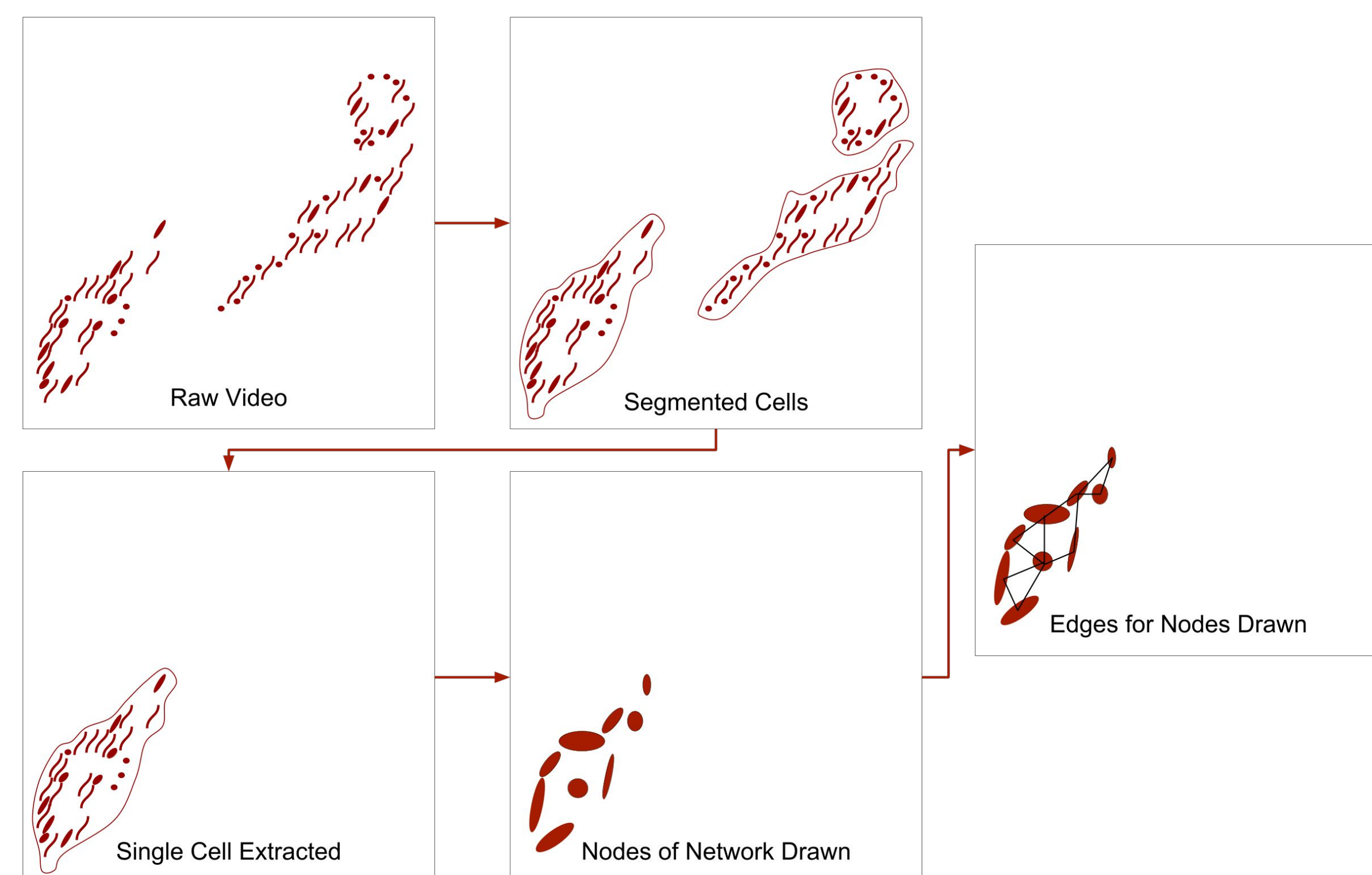




Goal

Using graph theory, develop a novel spatiotemporal model of subcellular evolution as it responds to environmental stimuli such as drugs or pathogens

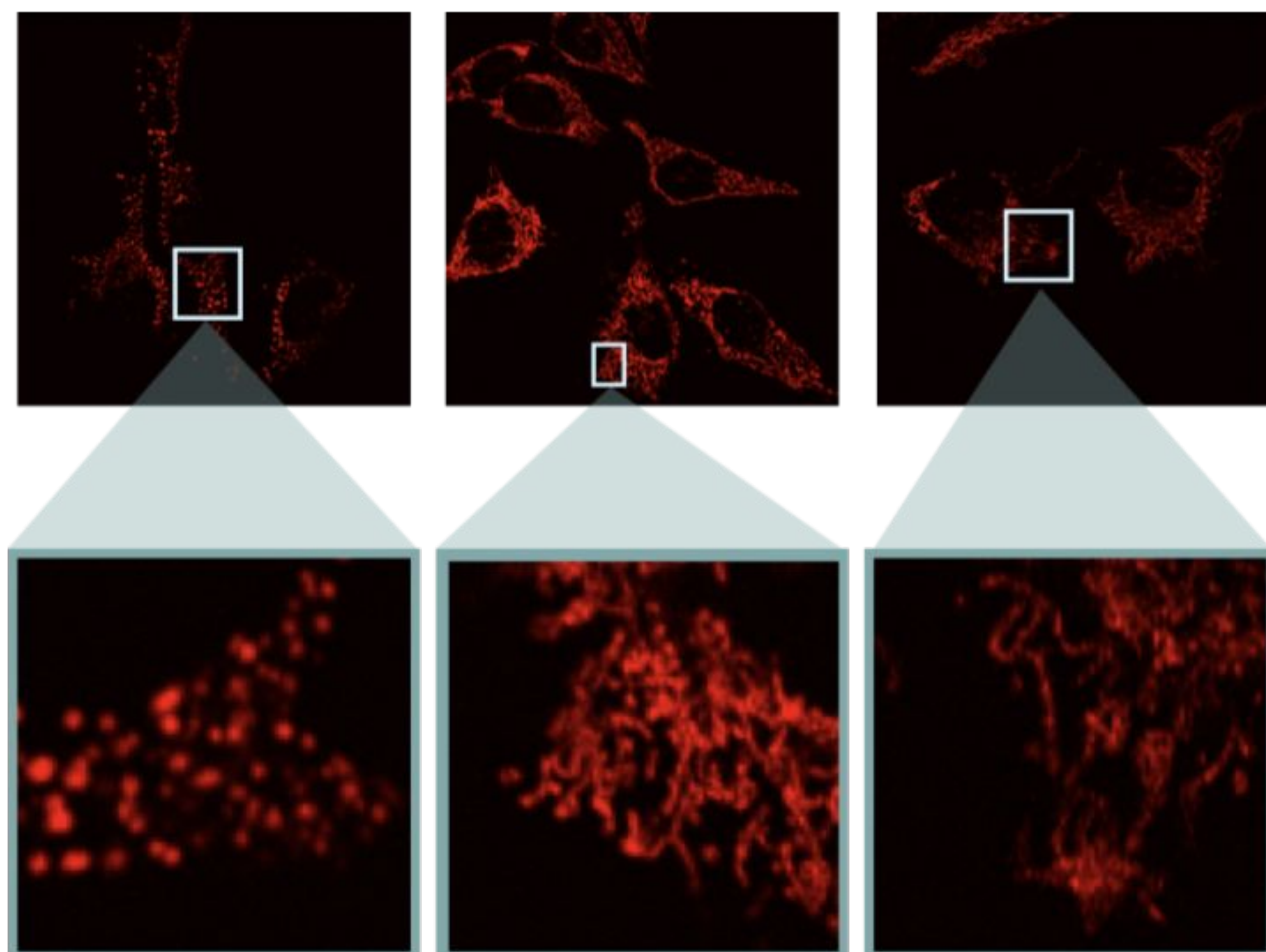
Proposed Pipeline



First, we segment the cells from the raw time-lapse video, analyzing each cell in isolation. Second, we build graph structures from the mitochondrial protein patterns. Third, we learn a mixture model and derive the weights between graph vertices from this model. This process is repeated for each frame in a video to capture the change in the model parameters.

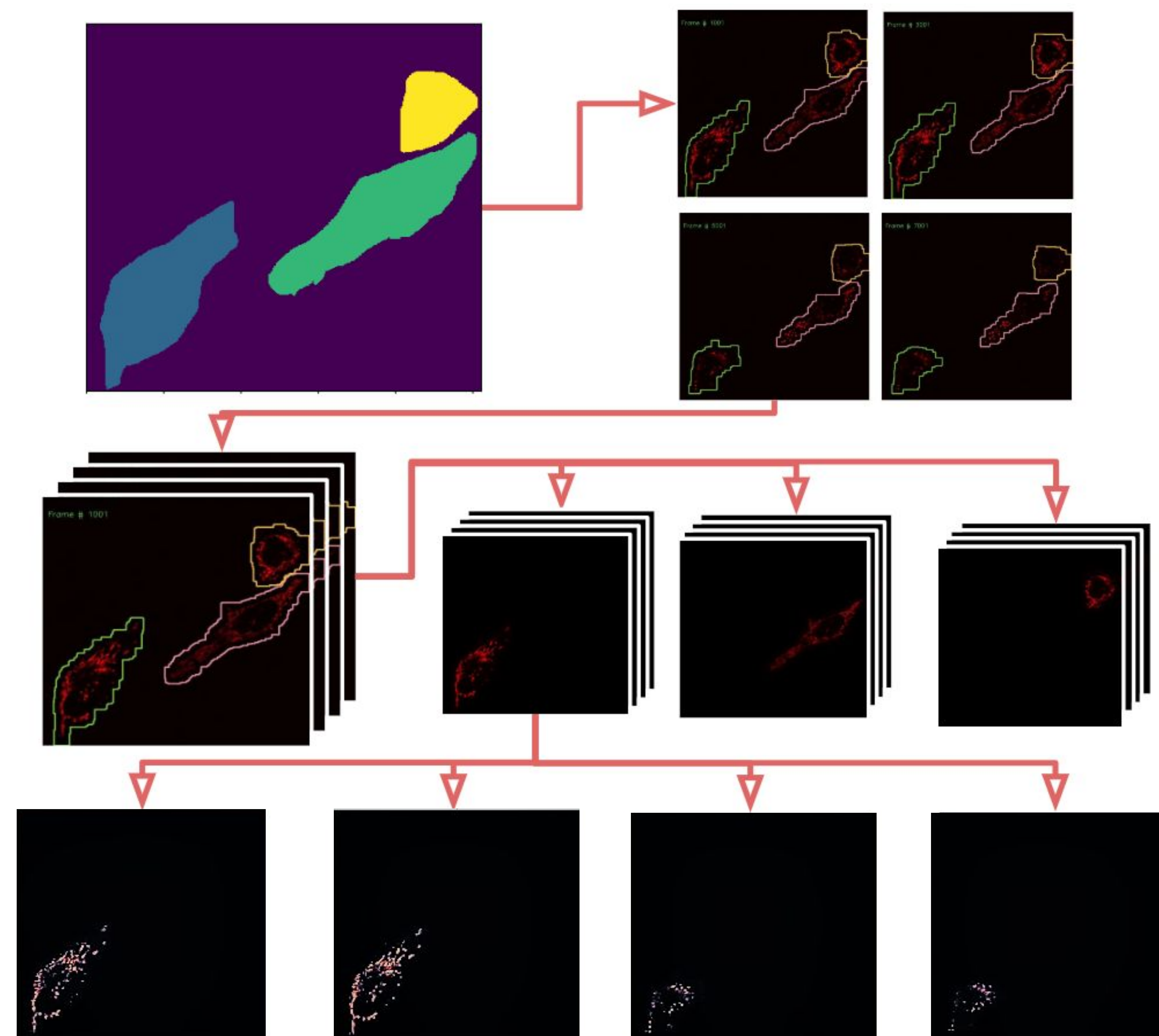
Data

Timelapse footage of mitochondria protein patterns in HeLa cells in three categories based on introduced morphology altering factors



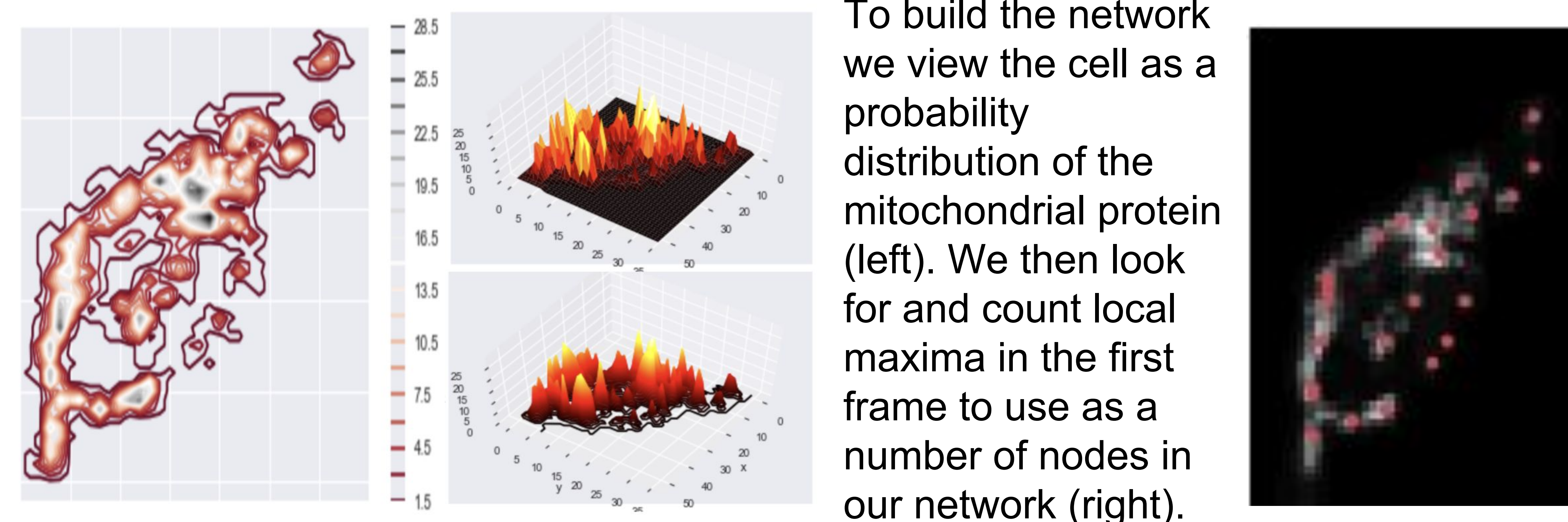
(Left) LLO induced mitochondrial fragmentation (Center) Wild type HeLa mitochondrial morphology (Right) Mdivi-1 induced mitochondrial hyperfusion

Segmentation Process



We use a hand drawn segmentation (top left) of the first frame of the video to seed the automatic segmentation process (top right). We use the generated masks to split the video into single cell videos (mid). Then each frame of a cell's video can be viewed as an image (bottom)

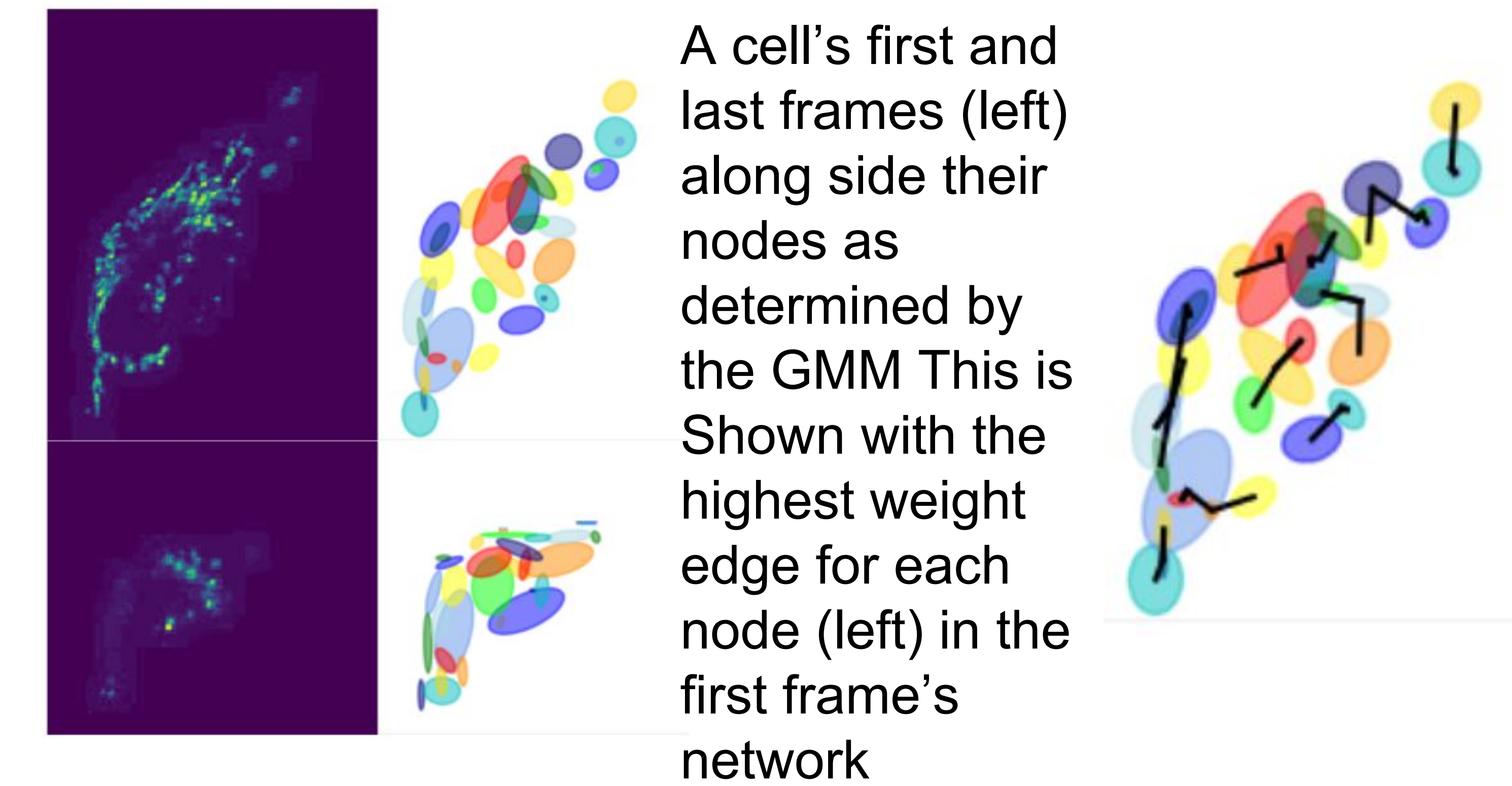
Social Network Construction



To build the network we view the cell as a probability distribution of the mitochondrial protein (left). We then look for and count local maxima in the first frame to use as a number of nodes in our network (right).

To place the nodes of the network model we apply a gaussian mixture model to each frame, and place a node at each gaussian in the mixture's mean. These are kept temporally linked by initializing each frame with the previous frame's nodes.

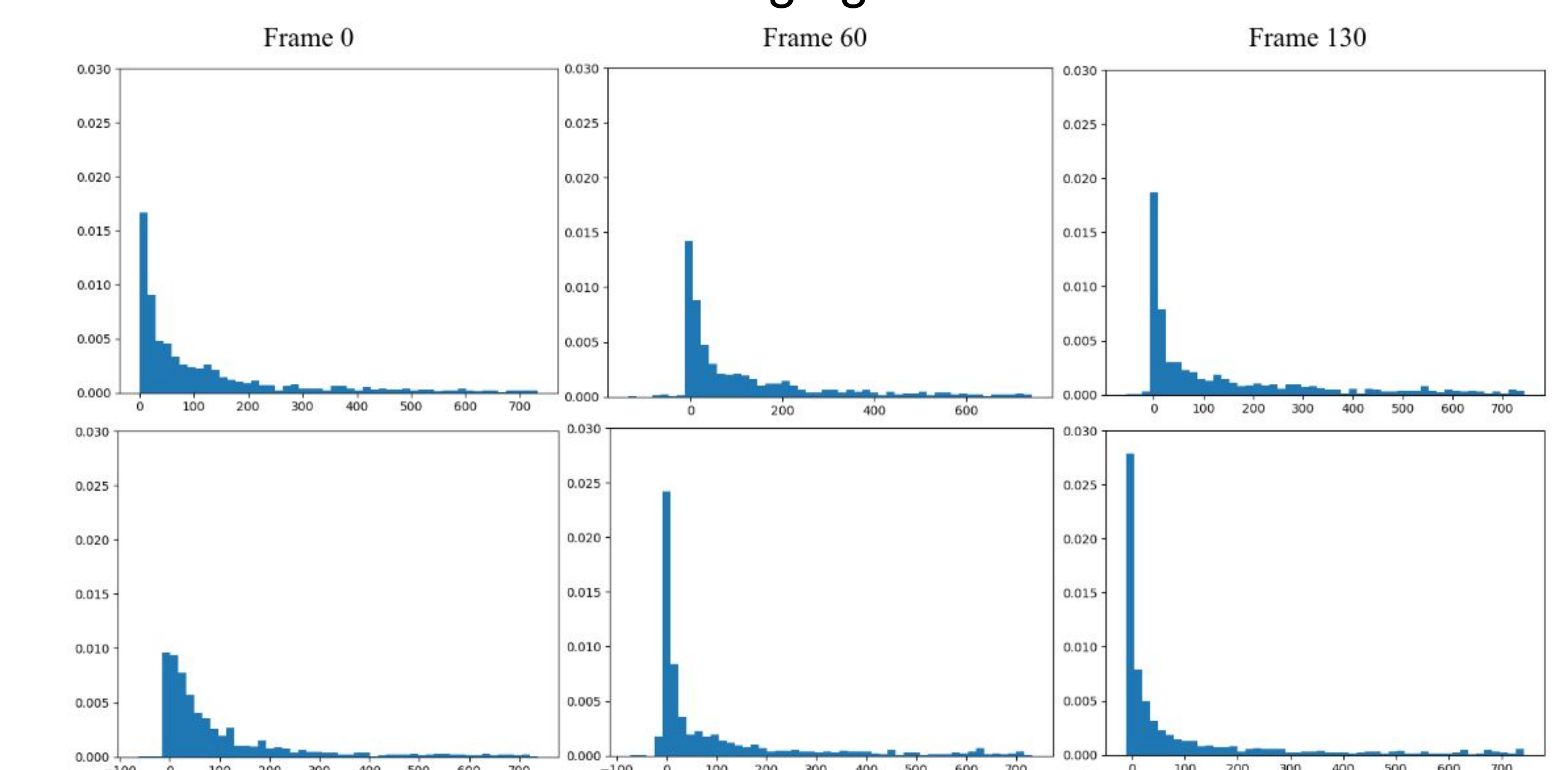
Social Network Construction cont.



To determine the affinity between nodes we evaluate the probability at node A's mean in the gaussian defined by node B as the weight of the edge from A -> B.

Conclusions and Future Work

We compared the the distribution of affinities over time in a control (top) and LLO fragmented (bottom) cell, showing the negative log of affinities in the first, middle, and last frames. We found a clear increase of connectivity in the network of the fragmenting cell which was absent in the unchanging control.



Moving forward we hope to improve the network generation process by adding a single uniform distribution to each network to account for background noise and work with alternate affinity functions like an implementation of the Kullback-Leibler (KL) divergence, which measures the difference between probability distributions. We will also employ additional graph analytics including common metrics like cliques and eigenvector centrality, and algorithms such as spectral clustering or PageRank for global network analysis. We also are looking into using laplacian gradients to observe temporal covariance of portions of the network model

References

"Large-scale Analysis of Spatiotemporal Organellar Network Evolution." *Quantitative Bioimaging Conference*, 2017.
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